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# A NEW GLUCOSIDE FROM WILLOW BARK.

BY

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LX.—*New Glucoside from Willow Bark.*

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It has been generally assumed that the different species of willow bark contain the same glucoside—salicin—although in varying amount. Beck, for example (*Amer. J. Pharm.*, 1891, 63, 581), gives the results of the assay of different species of willow bark, but no proof that the same glucoside was obtained from all the varieties. Having had occasion to examine a bark purchased as black willow, I found that the crystalline principle obtained from it by the usual method for preparing salicin, was not that substance, but a new glucoside for

which the name of *salinigrin* is provisionally proposed. Unfortunately, it has not been possible to determine with certainty from what species of *Salix* the bark was obtained, for the identification of the different species of willow, even in living plants, is admitted by botanists to be a most difficult task. Beck (*loc. cit.*) gives the yield of salicin from *Salix nigra* as 0·73 per cent. The determination of the constitution of this new glucoside has revealed an extremely interesting fact, for whilst salicin is the glucoside of *o*-hydroxybenzyl alcohol, salinigrin is the glucoside of *m*-hydroxybenzaldehyde, a substance not met with hitherto in plants.

A proximate analysis of the bark showed that, in addition to salinigrin, it contains a large amount of tannin, colouring matter, and the ordinary plant constituents. The amount of extractive matter obtained by means of alcohol and of water was 8·5 and 9·5 per cent. respectively.

#### *Preparation of Salinigrin.*

The coarsely powdered bark was boiled with a convenient quantity of water for 2 hours, the decoction strained, and the marc pressed. The aqueous extract was then evaporated to a somewhat low bulk, 10 per cent. of lead acetate added, the mixture boiled for a few minutes, and set aside. It was then strained through calico, the excess of lead acetate removed by hydrogen sulphide, and the mixture filtered. It was finally neutralised with ammonia, evaporated to a low bulk, and set aside to crystallise. The crystals were then drained by the aid of the pump, recrystallised from hot water until white, and finally recrystallised from hot alcohol. The yield of purified glucoside was about 1 per cent. of the bark, or somewhat higher than the figure given by Beck for salicin.

#### *Properties of Salinigrin.*

The glucoside separates in needles or rosettes, which, however, coalesce during collection and draining; if crystallised from water, it forms a crystalline mass; better crystals can be obtained from alcohol. The purity of the product was determined by the fact that, after five crystallisations from water, once from acetone and from alcohol, the melting point was unchanged. The crystals are anhydrous and melt at 195° (corr.) without decomposition, solidifying to a crystalline mass on cooling. It is fairly soluble in cold, and exceedingly soluble in hot water, sparingly soluble in cold, but more so in hot alcohol, also sparingly soluble in hot acetone, and almost insoluble in ether, light petroleum, or chloroform. Determinations of its solubility in water and in alcohol gave the following results:

1. In water at  $15^{\circ}$ : 7.5220 solution gave 0.1412 salt, hence 1 part is soluble in 52.2 parts of water.

2. In alcohol at  $15^{\circ}$ : 4.9980 solution gave 0.0228 salt, hence 1 part is soluble in 218.2 parts of alcohol.

The glucoside is lævorotatory, a determination of its specific rotation giving the following result:

$$\alpha_D = -3.5^{\circ}; l = 2 \text{ dm.}; c = 2.004; [\alpha]_D^{15} = -87.3^{\circ}.$$

Unlike salicin, it gives no colour reaction with sulphuric acid or with other reagents. It very slightly reduces Fehling's solution on boiling. On analysis, the following results were obtained:

0.255 gave 0.5178  $\text{CO}_2$  and 0.125  $\text{H}_2\text{O}$ .  $\text{C} = 55.37$ ;  $\text{H} = 5.45$ .

0.2308 „ 0.4664  $\text{CO}_2$  „ 0.117  $\text{H}_2\text{O}$ .  $\text{C} = 55.11$ ;  $\text{H} = 5.63$ .

$\text{C}_{13}\text{H}_{16}\text{O}_7$  requires  $\text{C} = 55.00$ ;  $\text{H} = 5.63$  per cent.

#### *Hydrolysis of Salinigrin.*

When salinigrin is boiled with dilute acids, it undergoes hydrolysis, glucose and *m*-hydroxybenzaldehyde being formed. The hydrolysis is best carried out as follows: 2 grams are dissolved in 50 c.c. of 3 per cent. aqueous sulphuric acid, the liquid boiled in a reflux apparatus for 3 to 4 hours, and then set aside. On cooling, long, needle-shaped crystals separate, which may be filtered off. The acid liquid is then extracted three or four times with ether, the ethereal solution washed, dried, and distilled. The crystalline residue is then mixed with the crystals previously separated, and the product set aside for further examination.

In two experiments, the yield of the product soluble in ether was determined with the following results:

(1). 2 grams gave 0.9396 gram. Yield = 46.98 per cent.

(2). 4 „ „ 1.8294 „ „ = 45.74 „

Calculated for *m*-hydroxybenzaldehyde = 47.7 per cent.

The liquid, after extraction with ether, is warmed, and then neutralised with barium carbonate, filtered, and the neutral filtrate evaporated to a low bulk on the water-bath. On standing and further evaporation, a syrup is formed which gradually crystallises and becomes a solid mass.

#### *A. Product Soluble in Ether.*

This, when first obtained, was slightly coloured and melted at  $105^{\circ}$ , but by recrystallising from water several times and decolorising with animal charcoal, long, needle-shaped crystals were obtained which, when dried at  $100^{\circ}$ , melted at  $108^{\circ}$  (corr.). The substance was only

slightly soluble in cold water, but freely so in alcohol, ether, chloroform, or benzene. The aqueous solution gave a violet coloration with ferric chloride and a precipitate with aqueous lead acetate solution. It also gave a precipitate with phenylhydrazine acetate and slightly reduced ammoniacal silver nitrate.

The air-dried crystals were found to contain  $\frac{3}{4}\text{H}_2\text{O}$ .

0.1506, at  $100^\circ$ , lost 0.0138  $\text{H}_2\text{O}$ .  $\text{H}_2\text{O} = 9.2$ .

$\text{C}_7\text{H}_6\text{O}_2 + \frac{3}{4}\text{H}_2\text{O}$  requires  $\text{H}_2\text{O} = 9.9$  per cent.

The anhydrous compound was analysed with the following results :

0.137 gave 0.346  $\text{CO}_2$  and 0.063  $\text{H}_2\text{O}$ .  $\text{C} = 68.87$  ;  $\text{H} = 5.03$ .

0.1594 ,, 0.4016  $\text{CO}_2$  ,, 0.0748  $\text{H}_2\text{O}$ .  $\text{C} = 68.71$  ;  $\text{H} = 5.2$ .

$\text{C}_7\text{H}_6\text{O}_2$  requires  $\text{C} = 68.85$  ;  $\text{H} = 4.92$  per cent.

These properties agree exactly with those recorded for *m*-hydroxybenzaldehyde, with the exception of the water of crystallisation and the melting point, the latter being given as  $104^\circ$ , whilst the purified hydrolytic product melted at  $108^\circ$  (corr.). This small difference is probably due to increased purity, as when first crystallised the substance melted at  $105^\circ$ .

Further proof of the identity of the product with *m*-hydroxybenzaldehyde was furnished by the preparation of the following derivatives :

The *phenylhydrazone*, prepared by Clemm's method (*Ber.*, 1891, 24, 826), melted, when first obtained, at  $130^\circ$ , the temperature given by Clemm, but on recrystallisation from hot benzene, fused at  $147^\circ$  (corr.). It was more easily prepared by warming an aqueous solution of the aldehyde with phenylhydrazine dissolved in glacial acetic acid, and then melted at  $147^\circ$  (corr.). On analysis :

0.1494 gave 17 c.c. moist nitrogen at  $13^\circ$  and 759 mm.  $\text{N} = 13.43$ .

$\text{C}_{13}\text{H}_{12}\text{ON}_2$  requires  $\text{N} = 13.20$  per cent.

It would appear, therefore, that the melting point as given by Clemm is too low.

The *oxime* was prepared in the usual way and separated from benzene as an oil which slowly solidified. The crystalline mass melted at  $87\text{--}88^\circ$ , as described by Dollfuss (*Ber.*, 1892, 25, 1924). On recrystallising this mass from benzene, long, needle-shaped crystals were obtained, which, after several recrystallisations, melted at  $138^\circ$  (corr.), and were analysed with the following result :

0.048 gave 4.4 c.c. moist nitrogen at  $15^\circ$  and 755 mm.  $\text{N} = 10.63$ .

$\text{C}_7\text{H}_7\text{O}_2\text{N}$  requires  $\text{N} = 10.2$  per cent.

Whether the higher melting point is due to increased purity of the product or to change into a stereoisomeride was not determined.

The *2-nitro-m-hydroxybenzaldehyde*, which crystallised in yellowish-

brown needles melting sharply at  $128^{\circ}$  (corr.), as described by Tiemann and Ludwig (*Ber.*, 1882, 15, 2052), and the *m*-hydroxybenzoic acid, which melted at  $200^{\circ}$  (corr.), were also prepared for purposes of comparison.

### B. Identification of the Sugar.

The crystalline mass which was obtained by the hydrolysis was dissolved in hot methyl alcohol and filtered. On evaporation, it gave a few needle-shaped crystals, which could not be separated, and on further evaporation the syrup first formed solidified as before. It was therefore dissolved in water, digested with a little animal charcoal, and the filtrate slowly evaporated. The usual crystalline mass was obtained, and this, while still pasty, was placed on a porous plate to remove the mother liquor. The crystals were then powdered and dried in a vacuum over sulphuric acid. The sugar had no sharp melting point, and was dextrorotatory; a determination of its specific rotation, after the solution had stood for several days, gave the following result:

$$\alpha_D = +2.1^{\circ}; l = 1 \text{ dcm.}; c = 4.14; [\alpha]_D = +50.7^{\circ}.$$

$$\text{For } d\text{-glucose, } \alpha_D = +52.7^{\circ}.$$

In the following qualitative reactions, the sugar behaved exactly like glucose; (i) it reduced Fehling's solution; (ii) with sodium *o*-nitrophenylpropionate, indigotin was obtained; (iii) with caustic soda, a reddish-brown coloration was produced; (iv) it gave the characteristic red colour with picric acid; and (v) charred only slowly with sulphuric acid.

Complete proof of its identity with *d*-glucose was furnished by the examination of the osazone. This was prepared in the usual way and was obtained in yellow crystals which melted at  $210^{\circ}$  (corr.) with decomposition. This is  $5^{\circ}$  higher than the melting point recorded for phenylglucosazone, but the melting points of this and of a specimen of phenylglucosazone, taken in the same bath, were found to be within one degree of each other. It has been pointed out (Beythien and Tollens, *Annalen*, 1889, 255, 217) that the melting points of osazones vary considerably, being dependent on the rate at which the bath is heated. The melting points just given were obtained by heating at an average rate. On analysis:

$$0.064 \text{ gave } 0.1412 \text{ CO}_2 \text{ and } 0.0366 \text{ H}_2\text{O. } C = 60.17; H = 6.34.$$

$$C_{18}H_{22}O_4N_4 \text{ requires } C = 60.33; H = 6.14 \text{ per cent.}$$

It is thus proved that salinigrin, on hydrolysis, yields quantitatively glucose and *m*-hydroxybenzaldehyde; its formula is therefore  $C_{13}H_{16}O_7$ . It can be easily distinguished from salicin by

affording with sulphuric acid a colourless solution, whilst salicin under similar conditions produces a blood-red colour. It would be possible to separate it from salicin by fractional crystallisation from alcohol, in which it is much the less soluble.

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